

Predictive value of a whole-blood Interferon- γ assay for the development of active tuberculosis disease after recent infection with *Mycobacterium tuberculosis*.

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A landmark trial comparing the accuracy of QuantiFERON®-TB Gold In-Tube (QFT™) to that of the tuberculin skin test (TST) in TB contacts.

Trial Facts

Objective

To compare—in a low-incidence setting—QFT and TST in recently exposed close contacts of active TB cases. The main objective was to look at the development of TB disease in these contacts within 2 years.

Trial design

Prospective trial.

Methodology

Close contacts of *M. tuberculosis*-positive source cases underwent both TST and QFT testing. Multivariate analysis was used to evaluate risk factors for *M. tuberculosis* infection. All patients were followed for two years to monitor whether any would develop TB disease.

Key inclusion criteria

Aggregate exposure time of the contact, prior to diagnosis of their respective index case, of not less than 40 hours in closed rooms.

Number of patients

601 contacts from 47 different culture-positive source cases.

Average length of follow-up

103 (±13.5) weeks.

Conclusion

“The high specificity of QFT and the high sensitivity of the test for those likely to progress, as suggested by our data, offer the possibility of limiting LTBI treatment to those truly infected. The high rate of progression to active TB of those QFT positive (14.6%) in our study, far greater than the 2.3% found for those TST positive, suggests significant health and economic implications for enhanced TB control”.

Diel et al AJRCCM 2008.¹⁹⁾

Major findings

1. QFT is more accurate than TST in predicting progression to TB disease.

	Positive Result	Progression rate of TB contacts to active disease at follow-up (2 year)
QFT	11% (66/601)	14.6%* (6 of 41 QFT positive contacts who declined treatment)
TST	40.4% (243/601) (at 5mm cut-off)	2.3%* (5 of 219 TST positive and untreated)

*(p<0.003)

- Isoniazid (INH) was only offered to QFT positive contacts, but was declined by 41 of the 66.
- Of the 41 who declined treatment, 6 developed active TB within two years, compared with none for the QFT-negative persons (181 were TST positive).
- Only 5 of the 6 (83%) who developed TB were TST positive.
- QFT detected all 6 contacts (100%) who later developed TB and established a positive predictive value of 14.6% for progression to TB within two years of infection. The corresponding value for the conventional skin test was 2.3%.
- In this study none of the 181 subjects who were TST positive, but QFT negative—and not given INH prophylaxis—progressed to active TB disease (after 2 years). The negative predictive value of QFT in this setting was thus 100%.
- These results are consistent with a Japanese study, where none of 91 TST positive /QFT negative contacts, not given INH prophylaxis, developed active TB during 3.5 years of follow-up.⁽²⁾

2. QFT positivity was associated with exposure time; TST positivity was not.

	Exposure time (hrs)
QFT	222.7 ± 237.4
TST	130.7 ± 147.0

*(p<0.0001⁽¹⁾)

- This result is in agreement with numerous other studies that QFT has better correlation with exposure time to index cases, as compared to the TST.^(3,4,5,6,7)

3. Reduction in the number of candidates for INH therapy by as much as 75%.

- 66 contacts were identified by QFT for INH therapy vs. 243 suggested by the TST.⁽¹⁾

“By using QFT as the standard by which INH is prescribed, use of that drug, with its risk of hepatotoxicity and other side effects, could be reduced by as much as 75%.”⁽¹⁾

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